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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NUMBER:	**10/510,667**
FILING DATE:	**October 7, 2004**
FIRST NAMED INVENTOR:	**Vasulinga Ravikumar**
ART UNIT:	**To Be Determined**
EXAMINER NAME:	**To Be Determined**
ATTORNEY DOCKET NUMBER:	**ISIS-5582**
TITLE:	**OLIGOMERIC COMPOUNDS HAVING MODIFIED PHOSPHATE GROUPS**

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Dated: 5/5/2005 By: Kemlyn Evans
Kemlyn Evans

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INFORMATION DISCLOSURE STATEMENT
Under 37 C.F.R. §§ 1.56 and 1.97-98

SIR:

Pursuant to the provisions of 37 C.F.R. §§ 1.56 and 1.97-98, enclosed herewith is PTO Form PTO/SB/08A and PTO/SB/08B listing references for consideration by the Examiner.

The filing of this Information Disclosure Statement shall not be construed as a representation regarding the completeness of the list of references, or that inclusion of a reference in this list is an admission that it is prior art or is pertinent to this application, or that a search has been made, or as an admission that the information listed is, or may be considered to be, material to patentability, or that no other material information exists, and shall not be construed as an admission against interest in any manner.

This Information Disclosure Statement is being filed:

☒ within three months of the filing date of the application, or date of entry into the national stage of an international application, or before the mailing date of a first office action on the merits, whichever event last occurred;

☐ before the mailing of a first official action after filing of a request for continued examination (RCE) under 37 C.F.R. § 1.114;

☐ after three months of the filing date of this national application or the date of entry of the national stage in an international application, or after the mailing date of the first official action on the merits, whichever event last occurred, but before that mailing date of the first office action to occur of either: (1) a final action under 37 C.F.R. § 1.113; or (2) an action that otherwise closes prosecution in the application, and:

☐ attached hereto is the fee set forth under 37 C.F.R. § 1.17(p) for submission of this Information Disclosure Statement under 37 C.F.R. § 1.97(c); OR

☐ Applicant certifies pursuant to 37 C.F.R. § 1.97(e) that:

☐ each item of the information contained in this Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Statement;

OR

☐ no item of information contained in this Information Disclosure Statement was cited in a counterpart foreign application and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in this Statement was known to any individual designated under 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Statement.

☐ on or before the payment of the issue fee but after the mailing date of the first to occur of either: (1) a final action under 37 C.F.R. § 1.113; (2) a notice of allowance under 37 C.F.R. § 1.311; or (3) an action that otherwise closes prosecution in the application, and:

☐ Applicant certifies pursuant to 37 C.F.R. § 1.97(e) that:

☐ each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement;

OR

☐ no item of information contained in this Information Disclosure Statement was cited in a counterpart foreign application and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in this Statement was known to any individual designated under 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Statement. AND

☐ attached hereto is the fee set forth under 37 C.F.R. § 1.17(p) for submission of this Information Disclosure Statement under 37 C.F.R. § 1.97(c); OR

☐ after the payment of the issue fee. Applicant requests that the information contained in this Information Disclosure Statement be placed in the file according to 37 C.F.R. § 1.97(i), although the information may not be considered by the USPTO.

☒ Enclosed is a copy of each listed reference that may be material to the examination of this application, and for which there may be a duty to disclose.

☐ This application relies, under 35 U.S.C. § 120, on the earlier filing date of prior application No. , filed on , and the references cited therein are hereby referenced, but are not required to be provided in this application under 37 C.F.R. § 1.98(d).

☒ This application was filed after June 30, 2003. Therefore, pursuant to the waiver of the requirements under 37 C.F.R. § 1.98(a)(2)(i), copies of each U.S. Patent and each U.S. Patent Application Publication are not required to be submitted. Copies of any foreign patent documents and non-patent literature cited herein are enclosed.

☐ Each item of information contained in this Information Disclosure Statement was cited in the communication from a foreign patent office in a counterpart application, and the communication was not received by any individual designated in 37 C.F.R. § 1.56(c) more than thirty days prior to the filing of this Information Disclosure Statement 37 C.F.R. § 1.704(d).

☒ Applicant submits that no fee is required for the consideration of this Information Disclosure Statement. However, if a fee is due, the Commissioner is hereby authorized to charge Deposit Account No 500252 referencing case number ISIS-5582.

Consideration of the listed references and favorable action are solicited.

Respectively Submitted,

Robert S. Andrews Dated: 5-5-05

Robert S. Andrews
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 7

Complete if Known	
Application Number	10/510,667
Filing Date	October 7, 2004
First Named Inventor	Vasulinga Ravikumar
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	ISIS-5582

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No.[1]	Document Number Number - Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	AA	US-6,033,909	03-07-2000	Uhlmann et al.	
	AB	US-09/115,043			

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3] - Number[4] - Kind Code[5] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]

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Sheet 2 of 7

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Art Unit	To Be Determined
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NON PATENT LITERATURE DOCUMENTS

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	AC	ALEFELDER, S. et al., "Incorporation of terminal phosphorothioates into oligonucleotides," *Nucleic Acids Res.* (1998) 26(21): 4983-4988.	
	AD	ALTMANN, K.-H. et al., "Second Generation of Antisense Oligonucleotides: From Nuclease Resistance to Biological Efficacy in Animals," *Chimia* (1996) 50: 168-176.	
	AE	ALTMANN, K.-H. et al., "Second-generation antisense oligonucleotides: structure-activity relationships and the design of improved signal-transduction inhibitors," *Biochem. Soc. Trans.* (1996) 24: 630-637.	
	AF	ALTMANN, K.-H. et al., "Second Generation Antisense Oligonucleotides – Inhibition of PKC-a and *c-RAF* Kinase Expression by Chimeric Oligonucleotides Incorporating 6'-Substituted Carbocyclic Nucleosides and 2'-O-Ethylene Glycol Substituted Ribonucleosides," *Nucleosides Nucleotides* (1997) 16(7-9): 917-926.	
	AG	BAKER, B. F. et al., "2'-O-(2-Methoxy)ethyl-modified Anti-intercellular Adhesion Molecule 1 (ICAM-1) Oligonucleotides Selectively Increase the ICAM-1 mRNA Level and Inhibit Formation of the ICAM-1 Translation Initiation Complex in Human Umbilical Vein Endothelial Cells," *J. Biol. Chem.* (1997) 272(18): 11944-12000.	
	AH	BEAL, P. A. et al., "Second Structural Motif for Recognition of DNA by Oligonucleotide-Directed Triple-Helix Formation," *Science* (1991) 251: 1360-1363.	
	AI	BOCK, L. C. et al., "Selection of single-stranded DNA molecules that bind and inhibit human thrombin," *Nature* (1992) 355: 564-566.	
	AJ	CHERUVALLATH, Z. S. et al., "A Novel Solid Support for Synthesis of Oligonucleotide 3'-Phosphorothioate Monoesters," *Bioorg. Med. Chem. Lett.* (2003) 13(2): 281-284.	
	AK	CHIANG, M.-Y. et al., "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule 1 Expression by Two Distinct Mechanisms," *J. Biol. Chem.* (1991) 266(27): 18162-18171.	
*	AL	COHEN, J. in *Oligonucleotides: Antisense Inhibitors of Gene Expression* (1989) CRC Press, Inc., Boca Raton, FL.	
	AM	COOK, P. D., "Medicinal chemistry of antisense oligonucleotides – future opportunities," *Anti-Cancer Drug Des.* (1991) 6: 585-607.	
	AN	CONTE, M. R. et al., "Conformational properties and thermodynamics of the RNA duplex r(CGCAAAUUUGCG)$_2$: comparison with the DNA analogue d(CGCAAATTTGCG)$_2$," *Nucleic Acids Res.* (1997) 25(13): 2627-2634.	

* A copy of these references will not be forwarded to the U.S. Patent and Trademark Office since it is believed to be too voluminous and easily obtainable by the Examiner.

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This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Sheet 3 of 7

Complete if Known	
Application Number	10/510,667
Filing Date	October 7, 2004
First Named Inventor	Vasulinga Ravikumar
Art Unit	To Be Determined
Examiner Name	To Be Determined
Attorney Docket Number	ISIS-5582

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T [2]
	AO	CROOKE, S. T., "Progress in Antisense Therapeutics," *Med Res. Rev.* (1996) 16(4): 319-344.	
	AP	CROOKE, S. T. et al., "Pharmacokinetic Properties of Several Novel Oligonucleotide Analogs in Mice," *J. Pharmacol. Exp. Ther.* (1996) 277(2): 923-937.	
	AQ	DELGADO, C. et al., "The Uses and Properties of PEG-Linked Proteins," *Crit. Rev. Ther. Drug Carr. Sys.* (1992) 9(3,4): 249-304.	
	AR	DE MESMAEKER, A. et al., "Antisense Oligonucleotides," *Acc. Chem. Res.* (1995) 28: 366-374.	
	AS	EGLI, M. et al., "RNA Hydration: A Detailed Look," *Biochem.* (1996) 35(26): 8489-8494.	
	AT	FEDOROFF, O. Y. et al., "Structure of a DNA:RNA Hybrid Duplex Why RNase H Does Not Cleave Pure RNA," *J. Mol. Biol.* (1993) 233: 509-523.	
	AU	FREIER, S. M. et al., "The ups and downs of nucleic acid duplex stability: structure-stability studies on chemically-modified DNA:RNA duplexes," *Nucleic Acids Res.* (1997) 25(22):4429-4443.	
	AV	GONZÁLEZ, C. et al., "Structure and Dynamics of a DNA·RNA Hybrid Duplex with a Chiral Phosphorothioate Moiety: NMR and Molecular Dynamics with Conventional and Time-Average Restraints," *Biochem.* (1995) 34(15): 4969-4982.	
	AW	GRIFFIN, L. C. et al., "In Vivo Anticoagulant Properties of a Novel Nucleotide-Based Thrombin Inhibitor and Demonstration of Regional Anticoagulation in Extracorporeal Circuits," *Blood* (1993) 81(12): 3271-3276.	
	AX	HAKIMELAHI, G. H. et al., "New catalysts and procedures for the dimethoxytritylation and selective silylation of ribonucleosides," *Can. J. Chem.* (1982) 60: 1106-1113.	
	AY	HAMM, M. L. et al., "Incorporation of 2'-Deoxy-2'-mercaptocytidine into Oligonucleotides via Phosphoramidite Chemistry," *J. Org. Chem.* (1997) 62(10): 3415-3420.	
	AZ	HORTON, N. C. et al., "The Structure of an RNA/DNA Hybrid: A Substrate of the Ribonuclease Activity of HIV-1 Reverse Transcriptase," *J. Mol. Biol.* (1996) 264: 521-533	
	BA	JONES, L. J., et al., "RNA Quantitation by Fluorescence –Based Solution Assay: RiboGreen Reagent Characterization," *Anal. Biochem.* (1998) 265: 368-374.	

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	BB	KABANOV, A. V. et al., "A new class of antivirals: antisense oligonucleotides combined with a hydrophobic subsituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells," *FEBS Lett.* (1990) 259(2): 327-330.	
	BC	KAWASAKI, A. M. et al., "Uniformly Modified 2'-Deoxy-2'-fluoro Phosphorothioate Oligonucleotides as Nuclease-Resistant Antisense Compounds with High Affinity and Specificity for RNA Targets," *J. Med. Chem.* (1993) 36(7): 831-841.	
	BD	LANE, A. N. et al., "NMR assignments and solution conformation of the DNA·RNA hybrid duplex d(GTGAACTT)·r(AAGUUCAC)," *Eur. J. Biochem.* (1993) 215: 297-306.	
	BE	LEFEBVRE, I. et al., "Mononucleoside Phosphotriester Derivatives with S-Acyl-2-thioethyl Bioreversible Phosphate-Protecting Groups: Intracellular Delivery of 3'-Azido-2',3'-dideoxythymidine 5'-Monophosphate," *J. Med. Chem.* (1995) 38(20): 3941-3950.	
	BF	LESNIK, E. A. et al., "Relative Thermodynamic Stability of DNA, RNA, and DNA:RNA Hybrid Duplexes: Relationship with Base Composition and Structure," *Biochem.* (1995) 34: 10807-10815.	
	BG	LETSINGER, R. L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties, and activity as inhibitors of replication of human immunodeficiency virus in cell culture," *Proc. Natl. Acad. Sci. USA* (1989) 86: 6553-6556.	
	BH	LORSCH, J. R. et al., "Reverse transcriptase reads through a 2'-5' linkage and a 2'-thiophosphate in a template," *Nucleic Acids Res.* (1995) 23(15): 2811-2814.	
	BI	MANOHARAN, M. et al., "Lipidic Nucleic Acids," *Tetrahedron Lett.* (1995) 36(21): 3651-3654.	
	BJ	MANOHARAN, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides," *Ann. N.Y. Acad. Sci.* (1992) 660: 306-309.	
	BK	MANOHARAN, M. et al., "Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents," *Nucleosides Nucleotides* (1995) 14(3-5): 969-973.	
	BL	MANOHARAN, M. et al., "Cholic Acid-Oligonucleotide Conjugates for Antisense Applications," *Bioorg. Med. Chem. Lett.* (1994) 4(8): 1053-1060.	
	BM	MANOHARAN, M. et al., "Introduction of Lipophilic Thioether Tehter in the Minor Groove of Nucleic Acids for Antisense Applications," *Bioorg. Med. Chem. Lett.* (1993) 3(12): 2765-2770.	

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	BN	MARTIN, P., "Ein neuer Zugang zu 2'-O-Alkylribonucleosiden und Eigenschaften deren Oligonucleotide," *Helv. Chim. Acta* (1995) 78: 486-504.	
	BO	MARTINEZ, J. et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi," *Cell* (2002) 110: 563-574.	
	BP	MEI, H.-Y. et al., "Tris9tetramethylphenanthroline)ruthenium(II): A chiral probe that cleaves A-DNA conformations," *Proc. Natl. Acad. Sci. USA* (1988) 85: 1349-1353.	
	BQ	MILLER, P. S. et al., "A new approach to chemotherapy based on molecular biology and nucleic acid chemistry: Matagen (masking tape for gene expression)," *Anti-Cancer Drug Design* (1987) 2:117-128.	
	BR	MILLIGAN, J. F. et al., "Current Concepts in Antisense Drug Design," *J. Med. Chem.* (1993) 36: 1923-1937.	
	BS	MISHRA, R. K. et al., "Improved leishmanicidal effect of phosphorotioate antisense oligonucleotides by LDL-mediated delivery," *Biochim. Biophys. Acta* (1995) 1264: 299-237.	
	BT	MONIA, B. P. et al., "Evaluation of 2'-Modified Oligonucleotides Containing 2'-Deoxy Gaps as Antisense Inhibitors of Gene Expression," *J. Biol. Chem.* (1993) 268(19): 14514-14522.	
	BU	OBERHAUSER, B. et al., "Effective incorporation of 2'-O-methyl-oligofibonucleotides into liposomes and enhanced cell association through modification with thiocholesterol," *Nucleic Acids Res.* (1992) 20(3): 533-538.	
	BV	OUCHI, T. et al., "Synthesis and Antitumor Activity of Poly(Ethylene Glycol)s Linked to 5-Fluorouracil via a Urethane or Urea Bond," *Drug Design and Delivery* (1992) 9: 93-105.	
	BW	POLUSHIN, N. N. et al., "Synthesis of Oligonucleotides Containing 2'-Azido- and 2'-Amino-2'-deoxyuridine Using Phosphotriester Chemistry," *Tetrahedron Lett.* (1996) 37(19): 3227-3230.	
	BX	RAVASIO, N. et al., "Selective Hydrogenations Promoted by Copper Catalysts. 1. Chemoselectivity, Regioselectivity, and Stereoselectivity in the Hydrogenation of 3-Substituted Steroids," *J. Org. Chem.* (1991) 56(13): 4329-4333.	
	BY	ROLAND, A. et al., "A novel linker for the solid-phase synthesis of a library of 3'-thiophosphoryated dinucleotides," *Tetrahedron Lett.* (2001) 42: 3669-3672.	
	BZ	SAISON-BEHMOARAS, T. et al., "Short modified antisense oligonucleotides directed against Ha-*ras* point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation," *EMBO J.* (1991) 10(5): 1111-1118.	

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*	CA	SANGER et al., *Principles of Nucleic Acid Structure* (1984) Springer Verlag, New York, NY.	
	CB	SCHWARZ, D. S. et al., "Evidence that siRNAs Function as Guides, Not Primers, in the *Drosophila* and Human RNAi Pathways," *Mol. Cell* (2002) 10: 537-548.	
	CC	SEARLE, M. S. et al., "On the stability of nucleic acid structures in solution: enthalpy – entropy compensations, internal rotations and reversibility," *Nucleic Acids Res.* (1993) 21(9): 2051-2056.	
	CD	SHEA, R. G. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucleotide conjugates," *Nucleic Acids Res.* (1990) 18(13): 3777-3783.	
	CE	STEIN, C. A. et al., "Oligodeoxynucleotides as Inhibitors of Gene Expression: A Review," *Cancer Res.* (1988) 48: 2659-2668.	
	CF	SVINARCHUK, F. P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups," *Biochimie* (1993) 75: 49-54.	
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* A copy of these references will not be forwarded to the U.S. Patent and Trademark Office since it is believed to be too voluminous and easily obtainable by the Examiner.

Examiner Signature		Date Considered	

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